

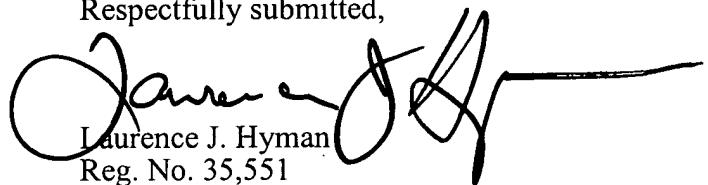
ROSE *et al.*
Application No.: 09/832,510
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PATENT

Amendment as an Appendix entitled "PENDING CLAIMS WITH ENTRY OF THE AMENDMENT."

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 21 of page 2 has been amended as follows:

In one embodiment, the peptide of the invention has a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is selected from the group consisting of all amino acids; R₅ is Ala; R₆ and R₇ are members independently selected from the group consisting of all amino acids; R₈ is Thr; R₉ is selected from the group consisting of all amino acids; R₁₀ is Cys; R₁₁, R₁₂, R₁₃, R₁₄, and R₁₅ are members independently selected from the group consisting of all amino acids; and, R₁₆ is Val (SEQ ID NO:1). In a preferred embodiment, the immunogenic peptide comprises a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

Paragraph beginning at line 4 of page 3 has been amended as follows:

The invention also provides a method for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody. The method of the invention comprises contacting the sample with an oligonucleotide primer pair capable of amplifying a subsequence of an MHC nucleic acid, which subsequence encodes a polypeptide comprising a peptide of the invention, as described above; amplifying the nucleic acid; and, detecting the amplified nucleic acid. In alternative embodiments, the MHC gene is HLA-DR 10 and the subsequence encodes a peptide wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is

Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

Paragraph beginning at line 22 of page 3 has been amended as follows:

The invention further provides a kit for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody. The kit comprises an oligonucleotide primer pair capable of amplifying a subsequence of an MHC gene or gene product, which subsequence encodes a polypeptide comprising a peptide of the invention. In alternative embodiments, the MHC gene can be HLA-DR 10; and, the peptide can comprise a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

Paragraph beginning at line 1 of page 4 has been amended as follows:

The invention also provides a method for detecting an antibody reactive with a non-Hodgkin's B cell lymphoma (B-NHL) cell. The method comprises contacting a sample, which can be a biological sample, with a composition of the invention under immunologically reactive conditions, and then detecting whether an antibody has specifically bound to the composition. In one embodiment, the composition comprises a peptide having a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2). In various embodiments of this method, the antibody is generated by a recombinant nucleic acid library, the recombinant nucleic acid is a phage display library, and the composition is fixed to a solid surface.

Paragraph beginning at line 11 of page 4 has been amended as follows:

The invention further provides a method for generating an antibody reactive with a non-Hodgkin's B cell lymphoma (B-NHL) cell. The method comprises administering an immunogenically effective amount of a composition of the invention to a mammal. The composition can comprise a peptide having a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2). The B-NHL cell can be a B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CCL/SLL) cell, a lymphoplasmacytoid lymphoma (LPL) cell, a follicular lymphoma (FL) cell, a mucosa-associated lymphoid tissue lymphoma (MALT) cell, a splenic lymphoma with villous lymphocytes (SLVL) cell and a mantle cell lymphoma cell.

Paragraph beginning at line 21 of page 4 has been amended as follows:

The invention provides an immunogenic composition capable of eliciting an immunogenic response directed to a polypeptide epitope, wherein the epitope comprises an amino acid sequence having a structure comprising R₁ - R₂ - R₃ - R₄ - R₅ - R₆ - R₇ - R₈ - R₉ - R₁₀ - R₁₁ - R₁₂ - R₁₃ - R₁₄ - R₁₅ - R₁₆, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ and R₄ are members independently selected from the group consisting of all amino acids; R₅ is Ala, Glu, Asp, Val, Leu or Ile; R₆ and R₇ are members independently selected from the group consisting of all amino acids; R₈ is Thr; R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, and R₁₅ are members independently selected from the group consisting of all amino acids; and, R₁₆ is Val. In one embodiment, the epitope comprises a sequence wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2). The immunogenic response can generate antibodies (i.e., a

humoral response) specific for the polypeptide epitope. Alternatively, the immunogenic response can generate an epitope specific cellular response.

Paragraph beginning at line 1 of page 5 has been amended as follows:

The invention further provides a method of inducing an immunogenic response directed to a polypeptide epitope, comprising administering an immunogenically effective amount of a composition comprising a polypeptide epitope to a mammal, wherein the epitope comprises an amino acid sequence having a structure comprising R₁ - R₂ - R₃ - R₄ - R₅ - R₆ - R₇ - R₈ - R₉ - R₁₀ - R₁₁ - R₁₂ - R₁₃ - R₁₄ - R₁₅ - R₁₆, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ and R₄ are members independently selected from the group consisting of all amino acids; R₅ is Ala, Glu, Asp, Val, Leu or Ile; R₆ and R₇ are members independently selected from the group consisting of all amino acids; R₈ is Thr; R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, and R₁₅ are members independently selected from the group consisting of all amino acids; and, R₁₆ is Val. In one embodiment, the epitope comprises an amino acid sequence having a structure wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2). The immunogenic response can generate antibodies (*i.e.*, a humoral response) specific for the polypeptide epitope. Alternatively, the immunogenic response can generate an epitope specific cellular response. In various embodiments, the method involves administering the immunogenic composition to a human, a mouse or a rabbit.

Paragraph beginning at line 4 of page 19 has been amended as follows:

This invention has, for the first time, determined the epitope for the Lym-1 antibody on Class II DR10 polypeptides is R₁ - R₂ - R₃ - R₄ - R₅ - R₆ - R₇ - R₈ - R₉ - R₁₀ - R₁₁ - R₁₂ - R₁₃ - R₁₄ - R₁₅ - R₁₆, where R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is

His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val, or, simply: (Gln, Lys, or Arg) - Arg - Arg - Ala - Ala - Val - Asp - Thr - Tyr - Cys - Arg - His - Asn - Tyr - Gly - Val (SEQ ID NO:2), which correspond to residues 70 to 85 on the DR10 polypeptide. Based on the secondary structure of DR molecules proposed by Brown (1993) *supra*, (see Fig. 1), in DR10, the valine at residue 85 in proximity to the arginine at residue 71 (because of the secondary structure induced by the intrachain disulfide bond) corresponds to residue R₁₆ and residue R₂, respectively, of the epitope of the invention. Accordingly, in one embodiment, the invention provides a polypeptide or peptide composition which, in addition to having the above-described amino acid sequence, has a secondary structure in the same orientation with respect to each other as in the native molecule (estimated by the teaching of, *e.g.*, the DR structure proposed by Brown (1993) *supra*). One of skill can readily test whether (and to what degree, *i.e.*, what with what affinity) a peptide with a particular secondary structure binds to Lym-1 antibody.

In the Claims:

Claims 2, 3, 9, 17, 21, 26, 29 and 32 have been amended as follows:

2. (Amended) The composition of claim 1, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is selected from the group consisting of all amino acids; R₅ is Ala; R₆ and R₇ are members independently selected from the group consisting of all amino acids; R₈ is Thr; R₉ is selected from the group consisting of all amino acids; R₁₀ is Cys; R₁₁, R₁₂, R₁₃, R₁₄, and R₁₅ are members independently selected from the group consisting of all amino acids; and, R₁₆ is Val (SEQ ID NO:1).

3. (Amended) The composition of claim 2, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

9. (Amended) The method of claim 7, wherein the subsequence encodes a peptide wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

17. (Amended) The kit of claim 15, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

21. (Amended) The method of claim 19, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

26. (Amended) The method of claim 22, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

29. (Amended) The immunogenic composition of claim 28, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

32. (Amended) The method of claim 31, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

PENDING CLAIMS WITH ENTRY OF THE AMENDMENT

1. (As filed) A composition comprising an isolated or recombinant peptide comprising a subsequence of a Class II major histocompatibility molecule, wherein the peptide has the following properties,

(a) having a structure comprising

$R_1 - R_2 - R_3 - R_4 - R_5 - R_6 - R_7 - R_8 - R_9 - R_{10} - R_{11} - R_{12} - R_{13} - R_{14} - R_{15} - R_{16}$,

wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 and R_4 are members independently selected from the group consisting of all amino acids; R_5 is Ala, Glu, Asp, Val, Leu or Ile; R_6 and R_7 are members independently selected from the group consisting of all amino acids; R_8 is Thr; R_9 , R_{10} , R_{11} , R_{12} , R_{13} , R_{14} , and R_{15} are members independently selected from the group consisting of all amino acids; and, R_{16} is Val;

(b) capable of generating an immune response to a non-Hodgkin's B cell lymphoma cell.

2. (Amended) The composition of claim 1, wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 is Arg; R_4 is selected from the group consisting of all amino acids; R_5 is Ala; R_6 and R_7 are members independently selected from the group consisting of all amino acids; R_8 is Thr; R_9 is selected from the group consisting of all amino acids; R_{10} is Cys; R_{11} , R_{12} , R_{13} , R_{14} , and R_{15} are members independently selected from the group consisting of all amino acids; and, R_{16} is Val (SEQ ID NO:1).

3. (Amended) The composition of claim 2, wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 is Arg; R_4 is Ala; R_5 is Ala; R_6 is Val; R_7 is Asp; R_8 is Thr; R_9 is Tyr; R_{10} is Cys; R_{11} is Arg; R_{12} is His; R_{13} is Asn; R_{14} is Tyr; R_{15} is Gly, and R_{16} is Val (SEQ ID NO:2).

4. (As filed) The composition of claim 1, further comprising a pharmaceutically acceptable excipient.

5. (As filed) The composition of claim 1, further comprising an adjuvant.
6. (As filed) The composition of claim 1, wherein the non-Hodgkin's lymphoma cell is selected from the group consisting of a B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CCL/SLL) cell, a lymphoplasmacytoid lymphoma (LPL) cell, a follicular lymphoma (FL) cell, a mucosa-associated lymphoid tissue lymphoma (MALT) cell, a splenic lymphoma with villous lymphocytes (SLVL) cell and a mantle cell lymphoma cell.
7. (As filed) A method for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody, the method comprising the following steps:
 - (a) contacting the sample with an oligonucleotide primer pair capable of amplifying a subsequence of an MHC nucleic acid, which subsequence encodes a polypeptide comprising a peptide of claim 1,
 - (b) amplifying the nucleic acid; and
 - (c) detecting the amplified nucleic acid.
8. (As filed) The method of claim 7, wherein the MHC gene is HLA-DR 10.
9. (Amended) The method of claim 7, wherein the subsequence encodes a peptide wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).
10. (As filed) The method of claim 7, wherein the biological sample comprises a B cell.

11. (As filed) The method of claim 10, wherein the B cell is a B lymphocytic non-Hodgkin's lymphoma cell.
12. (As filed) The method of claim 11, wherein the non-Hodgkin's lymphoma cell is selected from the group consisting of a B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CCL/SLL) cell, a lymphoplasmacytoid lymphoma (LPL) cell, a follicular lymphoma (FL) cell, a mucosa-associated lymphoid tissue lymphoma (MALT) cell, a splenic lymphoma with villous lymphocytes (SLVL) cell and a mantle cell lymphoma cell.
13. (As filed) The method of claim 7, wherein the biological sample is a body fluid sample or a biopsy sample.
14. (As filed) The method of claim 13, wherein the body fluid sample is a blood sample.
15. (As filed) A kit for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody, comprising an oligonucleotide primer pair capable of amplifying a subsequence of an MHC gene or gene product, which subsequence encodes a polypeptide comprising a peptide of claim 1.
16. (As filed) The kit of claim 15, wherein the MHC gene is HLA-DR 10.
17. (Amended) The kit of claim 15, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

18. (As filed) The kit of claim 15, further comprising an instructional material teaching a use of the kit, wherein the instructional material indicates that the kit is used for the detection of nucleic acid encoding a peptide reactive with a Lym-1 antibody and that the polypeptide is associated with non-Hodgkin's B cell lymphomas.
19. (As filed) A method for detecting an antibody reactive with a non-Hodgkin's B cell lymphoma cell, comprising:
 - (a) contacting a sample with a composition of claim 1 under immunologically reactive conditions, and
 - (a) detecting whether an antibody has specifically bound to the composition.
20. (As filed) The method of claim 19, wherein the sample is a biological sample.
21. (Amended) The method of claim 19, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).
22. (As filed) The method of claim 19, wherein the antibody is generated by a recombinant nucleic acid library.
23. (As filed) The method of claim 22, wherein the recombinant nucleic acid is a phage display library.
24. (As filed) The method of claim 19, wherein the composition is fixed to a solid surface.
25. (As filed) A method for generating an antibody reactive with a non-Hodgkin's B cell lymphoma cell, comprising administering an immunogenically effective amount of a composition of claim 1 to a mammal.

26. (Amended) The method of claim 22, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

27. (As filed) The method of claim 25, wherein the non-Hodgkin's lymphoma cell is selected from the group consisting of a B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CCL/SLL) cell, a lymphoplasmacytoid lymphoma (LPL) cell, a follicular lymphoma (FL) cell, a mucosa-associated lymphoid tissue lymphoma (MALT-L) cell, a splenic lymphoma with villous lymphocytes (SLVL) cell and a mantle cell lymphoma cell.

28. (As filed) An immunogenic composition capable of eliciting an immunogenic response directed to a polypeptide epitope, wherein the epitope comprises an amino acid sequence having a structure comprising

R₁ - R₂ - R₃ - R₄ - R₅ - R₆ - R₇ - R₈ - R₉ - R₁₀ - R₁₁ - R₁₂ - R₁₃ - R₁₄ - R₁₅ - R₁₆,

wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ and R₄ are members independently selected from the group consisting of all amino acids; R₅ is Ala, Glu, Asp, Val, Leu or Ile; R₆ and R₇ are members independently selected from the group consisting of all amino acids; R₈ is Thr; R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, and R₁₅ are members independently selected from the group consisting of all amino acids; and, R₁₆ is Val.

29. (Amended) The immunogenic composition of claim 28, wherein R₁ is Gln, Lys, or Arg; R₂ is Arg; R₃ is Arg; R₄ is Ala; R₅ is Ala; R₆ is Val; R₇ is Asp; R₈ is Thr; R₉ is Tyr; R₁₀ is Cys; R₁₁ is Arg; R₁₂ is His; R₁₃ is Asn; R₁₄ is Tyr; R₁₅ is Gly, and R₁₆ is Val (SEQ ID NO:2).

30. (As filed) The immunogenic composition of claim 28, wherein the immunogenic response generates antibodies specific for the polypeptide epitope.

31. (As filed) A method of inducing an immunogenic response directed to a polypeptide epitope, comprising administering an immunogenically effective amount of a composition comprising a polypeptide epitope to a mammal,

wherein the epitope comprises an amino acid sequence having a structure comprising

$R_1 - R_2 - R_3 - R_4 - R_5 - R_6 - R_7 - R_8 - R_9 - R_{10} - R_{11} - R_{12} - R_{13} - R_{14} - R_{15} - R_{16}$,

wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 and R_4 are members independently selected from the group consisting of all amino acids; R_5 is Ala, Glu, Asp, Val, Leu or Ile; R_6 and R_7 are members independently selected from the group consisting of all amino acids; R_8 is Thr; R_9 , R_{10} , R_{11} , R_{12} , R_{13} , R_{14} , and R_{15} are members independently selected from the group consisting of all amino acids; and, R_{16} is Val.

32. (Amended) The method of claim 31, wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 is Arg; R_4 is Ala; R_5 is Ala; R_6 is Val; R_7 is Asp; R_8 is Thr; R_9 is Tyr; R_{10} is Cys; R_{11} is Arg; R_{12} is His; R_{13} is Asn; R_{14} is Tyr; R_{15} is Gly, and R_{16} is Val (SEQ ID NO:2).

33. (As filed) The immunogenic composition of claim 31, wherein the immunogenic response generates antibodies specific for the polypeptide epitope.

34. (As filed) The method of claim 31, wherein the mammal is a human, a mouse or a rabbit.